UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/003,869	01/07/1998	NIGEL ROBERT ARNOLD BEELEY	030639.0043.CPA1	9574

7590 11/04/2003

ARNOLD & PORTER
Attn: IP Docketing Department, Room 1126B
555 Twelfth Street, NW
Washington, DC 20004-1206

EXAMINER	
MOHAMED, ABDEL A	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 11/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/003,869	BEELEY ET AL.	
	Examin r	Art Unit	
	Abdel A. Mohamed	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 August 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35-104* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35-104* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

ACKNOWLEDGMENT OF AMENDMENT, REMARKS, STATUS OF THE APPLICATION AND CLAIMS

1. The amendment and remarks filed 8/29/03 are acknowledged, entered and considered. In view of Applicant's request the specification and the claims have been amended. Claims 1-34 have been canceled (although, claims 23-30 and 34 have been canceled previously on Paper No. 30, Amendment D, filed 11/13/02) and claims 35-104 (See Rule 126 below) have been added. Thus, claims 35-104 are now pending in the application. The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be renumbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not). Misnumbered claims 68-101 have been renumbered 70-104 because there were two sets of claims 68 and 69 (i.e., duplicates, See e.g., pages 5 and 6 of the amendment filed 8/29/03). Thus, claims 68-101 and dependents thereof have been corrected as claims 70-104 according to Rule 126. The objection to the claims is withdrawn in view of Applicant's amendment and remarks filed 8/29/03. However, the rejection under 35 U.S.C. 103(a) over the prior art of record for newly submitted claims 35-104 is maintained for the same reasons discussed in the previous Office action.

2. **CLAIMS REJECTION-35 U.S.C. §103(a)**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Newly submitted claims 35-104 (canceled claims 1-22 and 32-33) remain rejected under 35 U.S.C. 103(a) as being unpatentable over Navarro et al. (Journal of Neurochemistry, Vol. 67, No. 5, pp. 1982-1991, 1996) taken with Eng (U.S. Patent No. 5,424,286) and WO 96/40196.

Navarro et al. teach the intracerebroventricular (I.C.V.) administration of GLP-1 (7-36) amide in combination with exendin-3 and exendin-4 in a broad range of doses (0.2, 1, 5, 25, 100 and 500 ng) which resulted in marked decrease of both food and water intake (See e.g., abstract, page 1984, right column under Experimental Design, and page 1986, right column) as directed to newly submitted claims 35-44, 46, 48-49, 67-71, 73-82, 84 and 101-103. On page 1986, right column, the reference clearly shows that using *in vivo* system of both exendin-4 and exendin (9-39) interact with the GLP-receptor of the rat brain in proving that their use would result in controlling food and water intake that affect satiety reduced food intake and body weight in rodents.

The reference of Navarro et al. differs from newly submitted claims 35-104 failing to teach the use of various exendin and exendin antagonists including amylin agonist and CCK for treating conditions or disorders which include obesity, diabetes, eating disorders, insulin resistance syndrome, lowering the plasma glucose level, lowering the plasma lipid level, reducing the cardiac risk, and reducing the appetite of the subject. However, the secondary reference of Eng (U.S. Patent No. 5,424,286) teaches a pharmaceutical composition comprising exendin-3 or exendin-4, fragments thereof, or any combination thereof for treatment of diabetes mellitus and the prevention of hyperglycemia (See e.g., Abstract and Summary of the Invention) as directed to newly submitted claims 45, 47, 51-66, 83, and 85-100. The '286 patent on col. 4, lines 66 to col. 5, lines 19, states that the compounds of the present invention (i.e., exendin-3 and or exendin-4, or their functional derivatives combined in admixture with a pharmaceutically acceptable carrier vehicle) can be formulated according to known

methods to prepare pharmaceutically useful compositions which may be injected intravenously, intramuscularly, subcutaneously, or intraperitoneally, would call for dosages of about 0.1 pg/kg to 1,000 mg/kg body weight depending on many individual factors such as age, severity of disease, total body weight, sex, and other mitigating factors. Thus, clearly showing that the use of exendin-3 and exendin-4 as insulinotrophic agents for the treatment of diabetes mellitus and the prevention of hyperglycemia. Further, the patent of WO 96/40196 discloses compositions and methods for reducing food intake, suppressing appetite and controlling body weight by administering compositions comprising an amylin agonist and a CCK (See abstract and Summary of the Invention) as directed to newly submitted claims 50, 66, 72, 86, 100 and 104.

Thus, the secondary references clearly teach the use of exendin or exendin antagonist including amylin agonist and CCK for treatment of diabetes and prevention of hyperglycemia (i.e., lowering the plasma glucose level) and reducing food intake, suppressing appetite and controlling body weight. Although, the secondary reference of Eng does not teach a method for reducing food intake and body weight in a subject; however, such metabolic intervention intended to an effective treatment to reduce food intake and body weight is taught by the primary reference of Navarro et al., and the secondary reference of WO 96/40196. Therefore, given the teachings of the secondary reference of Eng, one of ordinary skill in the art would have been motivated to adapt the above scheme of using exendin or exendin antagonist alone or in combination with other compounds or composition that affect satiety, because such features are known in

the art. Hence, including such features into the composition of the primary reference in view of secondary references would have obvious to one having ordinary skill in the art to obtain the known and recognized functions and advantage thereof.

With respect to the amount of dosages, although each of the prior art clearly discloses the use of broad ranges of dosages; the prior art does not teach the dosages in the manner claimed; however, it would be conventional and within the ordinary skill in the art to which this invention pertains to select the appropriate optimum dosage of specific exendin or exendin antagonist peptide for the intended purpose of formulating a therapeutically effective pharmaceutical composition. Thus, in view of this, the subject composition may be used in combination with other materials to provide a wide variety of applications or may be tailored for specific applications, absence of sufficient objective factual evidence or unexpected results to the contrary.

ARGUMENTS ARE NOT PERSUASIVE

3. The rejection of newly submitted claims 35-104 (canceled claims 1-22 and 32-33) under 35 U.S.C. 103(a) as being unpatentable over Navarro et al. (Journal of Neurochemistry, Vol. 67, No. 5, pp. 1982-1991, 1996) taken with Eng (U.S. Patent No. 5,424,286) and WO 96/40196.

Applicant's arguments filed 8/29/03 have been fully considered but they are not persuasive. Applicant's arguments that the primary reference of Navarro et al. does not teach or disclose or suggest the use of exendin-3. Rather, Navarro discusses exendin-4 and exendin (9-39), which is a GLP-1 antagonist. Further, Applicant notes that

nowhere does Navarro disclose or suggest the combined use of GLP-1 (7-36) amide and exendin-4. Rather, Navarro discusses the I.C.V. administration of exendin-4 alone, i.e., not in combination with GLP-1 (7-36) is not persuasive. Contrary to Applicant's arguments, the features upon which Applicant relies (i.e., the combined use of GLP-1 (7-36) amide and exendin-4) are not recited in the newly submitted claims. Although, the Examiner assumes from the statement combined, Applicant intends to mean use and/or administration of one or more compounds selected from the group consisting of an amylin agonist, a leptin, and a cholecytokinin (CCK) as recited in claims 51, 66, 72, 86, 100 and 104. Although, the primary reference of Navarro et al. teach the intracerebroventricular (I.C.V.) administration of GLP-1 (7-36) amide in combination with exendin-3 and exendin-4 in a broad range of doses (0.2, 1, 5, 25, 100 and 500 ng) which resulted in marked decrease of both food and water intake (See e.g., abstract, page 1984, right column under Experimental Design, and page 1986, right column) as directed to newly submitted claims 35-44, 46, 48-49, 67-71, 73-82, 84 and 101-103. However, the limitations Applicant argued with (i.e., the combined use of GLP-1 (7-36) amide and exendin-4) are not recited in the rejected claim(s). Nevertheless, the claims are interpreted in light of the specification, limitation from specification are not read into claims. See *In re Van Geuns*, 988 F.2nd 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Thus, Applicant's arguments are not commensurate to the scope of the claims.

Further, Applicant asserts that Navarro does not disclose the peripheral administration of an exendin, much less the ability of exendins to reduce food intake, appetite, or a plasma lipid of a subject following peripheral administration. The

secondary references of Eng and WO 96/40196 do nothing to remedy the deficiencies of Navarro in this respect. Neither secondary reference teaches, discloses, or suggests the use or ability of exendins to reduce the food intake, appetite, or a plasma lipid level of a subject following peripheral administration. Contrary to Applicant's assertion, the secondary reference of Eng (U.S. Patent No. 5,424,286) teaches a pharmaceutical composition comprising exendin-3 or exendin-4, fragments thereof, or any combination thereof for treatment of diabetes mellitus and the prevention of hyperglycemia (See e.g., Abstract and Summary of the Invention) as directed to newly submitted claims 45, 47, 51-66, 83, and 85-100. The '286 patent on col. 4, lines 66 to col. 5, lines 19, states that the compounds of the present invention (i.e., exendin-3 and or exendin-4, or their functional derivatives combined in admixture with a pharmaceutically acceptable carrier vehicle) can be formulated according to known methods to prepare pharmaceutically useful compositions which may be injected intravenously, intramuscularly, subcutaneously, or intraperitoneally, would call for dosages of about 0.1 pg/kg to 1,000 mg/kg body weight depending on many individual factors such as age, severity of disease, total body weight, sex, and other mitigating factors. Thus, clearly showing that the use of exendin-3 and exendin-4 as insulinotrophic agents for the treatment of diabetes mellitus and the prevention of hyperglycemia. Further, the patent of WO 96/40196 discloses compositions and methods for reducing food intake, suppressing appetite and controlling body weight by administering compositions comprising an amylin agonist and a CCK (See abstract and Summary of the Invention) as directed to newly submitted claims 50, 66, 72, 86, 100 and 104.

Thus, the secondary references clearly teach the use of exendin or exendin antagonist including amylin agonist and CCK for treatment of diabetes and prevention of hyperglycemia (i.e., lowering the plasma glucose level) and reducing food intake, suppressing appetite and controlling body weight. Although, the secondary reference of Eng does not teach a method for reducing food intake and body weight in a subject; however, such metabolic intervention intended to an effective treatment to reduce food intake and body weight is taught by the primary reference of Navarro et al., and the secondary reference of WO 96/40196.

With respect to "peripheral administration", although, Applicant has not shown support for the limitation of the claims to "peripheral administration" as shown infra in the rejection under 35 U.S.C. 112, first paragraph for new matter. However, the term "peripheral" is defined or understood to mean "outer area of the visual field, i.e., auxiliary". Thus, in view of the common definition, all the parenteral administrations conducted by the references such as injections by intramuscularly or intravenously or subcutaneously or intraperitoneally are understood to include the term "peripheral administration", and as such, Applicant's arguments with respect to Peripheral administration are unpersuasive.

In regard to Applicant's arguments that in proper obviousness determination, the changes from the prior art must be evaluated in terms of the whole invention, including whether the prior art provides any teaching or suggestion to one of ordinary skill in the art to make the changes that would produce the claimed invention and cites *In re Chu*, 36 USPQ 2d 1089, 1094 (Fed. Cir. 1995). Further, Applicant continues by stating that

the Examiner's conclusion of obviousness is based on improper reasoning and mischaracterization of the art. No suggestion to modify the cited references has been found in the cited references or pointed out to Applicant from the general knowledge of one of ordinary skill in the art. For at least these reasons, the Examiner has failed to establish a *prima facie* case of obviousness, as required by 35 U.S.C. 103(a) is unpersuasive. Contrary to Applicant's arguments, in view of the combined teachings of the prior art and in view for the reasons discussed above; one of ordinary skill in the art would have been motivated at the time the invention was made to employ or use the subject composition in combination with other materials to provide a wide variety of applications or may be tailored for specific applications in the manner claimed. Thus, it is made obvious by the combined teachings of the prior art since the instantly claimed invention which falls within the scope of the prior art teachings would have been obvious because as held in host of cases including *Ex parte Harris*, 748 O.G. 586; *In re Rosselete*, 146 USPQ 183; *In re Burgess*, 149 USPQ 355 and as exemplified by *In re Betz*, "the test of obviousness is not express suggestion of the claimed invention in any and all of the references but rather what the references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them".

NEW GROUND OF REJECTION

The following is a new ground of rejection necessitated by Applicant's amendment.

CLAIMS REJECTION-35 U.S.C. § 112 1st PARAGRAPH

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 35-104 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Independent claims 35, 51, 67, 73, 87 and 101, and dependent claims 36, 37, 52, 53, 68, 69, 74, 75, 88, 89, 102 and 103 as amended on 8/29/03 contain new matter because the original specification does not appear to support **peripherally** administering or **peripheral** administration. Independent claims 35, 51, 67, 73, 87 and 101 have no support for **peripherally** administering, and dependent claims 36, 37, 52, 53, 68, 69, 74, 75, 88, 89, 102 and 103 have no support for **peripheral** administration from the original disclosure because there is no disclosure in the specification as now claimed. Thus, Applicant respectfully requested to either cancel all unsupported subject matter or to show where such subject matter has support from the original disclosure

ACTION IS FINAL, NECESSITATED BY AMENDMENT

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

CONCLUSION AND FUTURE CORRESPONDENCE

6. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (703) 308-3966. The examiner can normally be reached on Monday through Friday from 7:30 a.m. to 5:00 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (703) 308-2923. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306 for regular communications and (703) 305-7401 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Mohamed/AAM

October 28, 2003

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600